REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 5, 8, 15-27, 46, 52, 53 and 64-67 were previously pending in this application.

Claims 1, 2, 5, 8, 15, 16, 46 and 64 have been amended. Claim 1 has been amended to recite:

> A method of treating a disorder in a human subject comprising orally administering to the subject a polypeptide comprising one or more single domain antibodies, wherein at least one of the single domain antibodies is an anti-TNF-alpha single domain antibody that binds to human TNF-alpha and that comprises CDR 3 of a single domain antibody having the amino acid sequence of SEQ ID NO:12 or SEQ ID NO:13.

Support for this amendment is found throughout the instant specification, for example, at page 49, lines 19 to 23; at Example 4, starting at page 59, through Example 6 at page 62; at Example 24 at page 76; and at page 93, where SEQ ID NOs: 12 and 13 are disclosed. The other amended claims were amended to be consistent with the amendments made to claim 1 or to make minor clarifying amendments.

Claims 17-27, 52 and 53 were previously withdrawn and have now been canceled without prejudice or disclaimer. Claims 65 to 67 have been canceled without prejudice or disclaimer. Applicant reserves the right to pursue the subject matter of any of the canceled claims in one or more continuing applications.

Claim 68 has been added. Support for claim 68 can be found at least in claim 1 as originally filed.

Claims 1, 2, 5, 8, 15, 16, 46, 64 and 68 are pending for examination. No new matter has been added.

Objections to the Specification

The Examiner objected to the title and abstract because, according to the Examiner, neither disclose the subject matter of the instant claimed invention. Action at page 3. Applicant has amended the title and abstract to refer to the instant claimed invention.

Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

Priority

The Examiner questioned certain priority claims. Action at page 3. This issue is being considered, but the question of priority has no bearing on any arguments presented in this response.

Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement

The Examiner rejected claims 1, 2, 5, 8, 46 and 64-67 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Action at page 5. According to the Examiner, "[t]he claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *Id.* The Examiner stated that "Applicant has claimed broad methods of administering single domain antibodies to treat disorders. Neither the antigenic targets bond by the administered antibodies, nor the diseases and disorders being treated are recited in the instant claims." *Id.* The Examiner also stated that "a skilled artisan would be required to perform unpredictable experimentation in figuring out which antigenic targets are useful in which diseases prior to practicing the claimed methods." *Id.*

Solely to expedite prosecution, and not acquiescing to the rejection, claim 1 has been amended to recite that at least one single domain antibody is an anti-TNF-alpha single domain antibody that binds to human TNF-alpha. Thus, claim 1 now recites the particular target of at least one single domain antibody. All of the other remaining rejected claims ultimately depend from claim 1.

Those skilled in the art would be familiar with disorders that may be treated with anti-TNF antibodies. In fact, the Examiner stated that PCT Publication No. WO 97/29131 "disclose[s] methods of administering antibodies that bind human TNFα to treat numerous diseases and disorders, including intestinal disorders including Crohn's disease and ulcerative colitis . . . ." Action at page 9.

Thus, the enablement rejection has been obviated, and the specification would have enabled one skilled in the art to carry out the claimed methods. Accordingly, reconsideration and withdrawal of the enablement rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description

The Examiner rejected claims 1, 2, 5, 8, 15, 46, and 64-67 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Action at page 6. According to the Examiner, the claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention." *Id.*

The Examiner contended that "the size of the genus of antibodies used in the methods is large and reasonably unknowable since it encompasses antibodies to all possible targets for all possible diseases." *Id.* The Examiner noted that claim 15 further recites that the target is TNFα and that the disorder is inflammation. *Id.* The Examiner, however, contended that "the source of TNFα and the subject to whom the antibodies are administered is not recited." *Id.* at page 7. The Examiner further contended that "the specification indicates that 'targets' comprise not only

wild type sequences but additionally comprise fragments, truncations, insertions, deletions and mutations of said wild type targets . . . ." *Id.* The Examiner then alleged that in view of the breadth of such targets, "it is not reasonable that applicant is in possession of antibodies that bind the genus of all [such TNFα antigens]." *Id.* The Examiner concluded that "even the target 'TNFα" lacks adequate written description based upon the [breadth] that this genus encompasses . . . ." *Id.* at page 8.

Solely to expedite prosecution, and not acquiescing to the rejection, claim 1 has been amended to recite that at least one single domain antibody is an anti-TNF-alpha single domain antibody that binds to human TNF-alpha. Thus, claim 1 now recites the particular target of at least one single domain antibody. Claim 1 further has been amended to recite that the subject is human. All of the other remaining rejected claims ultimately depend from claim 1.

Thus, the Examiner's basis for the rejection, the alleged breadth of the claimed genus of TNF-alpha targets, is now moot. The specification clearly conveys that Applicant was in possession of the methods recited in the rejected claims. Accordingly, reconsideration and withdrawal of the written description rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claim 16 under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Action at page 8. According to the Examiner, claim 16 is unclear because the phrase "corresponds to a sequence represented by any of SEQ ID NOs:12 to 14" is unclear. *Id.*

Solely to expedite prosecution, and not acquiescing to the rejection, claim 16 has been amended to recite that the polypeptide comprises any one of SEQ ID NOs: 12 to 14, as suggested by the Examiner.

Thus, the rejection is moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 1, 2, 5, 8, 15, 46, and 64-67 under 35 U.S.C. § 102(b) as allegedly being anticipated by Salfeld et al. (WO 97/29131) ("Salfeld"). Action at page 9. The Examiner alleged that Salfeld discloses "methods of administering antibodies that bind human TNFα . . . ." *Id.* The Examiner further contended that Salfeld disclosed single chain Fv (scFv) as anti-TNFα antibodies. *Id.* Finally, citing the Background section of the instant specification, the Examiner contended that the instant specification defines single domain antibodies as encompassing scFv. *Id.*

At the outset, Applicant respectfully disagrees with the Examiner's contention that the instant specification defines single domain antibodies as encompassing scFv. Single domain antibodies are defined on page 13, lines 1 to 16, of the instant specification as follows: "Single domain antibodies are antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies."

The Examiner refers to lines 1 to 16 of page 1 of the instant application to try to support the argument that the instant application teaches that scFv antibodies are single domain antibodies. However, the paragraph referred to by the Examiner is in the Background section and does not refer to the single domain antibodies, but rather refers to "conventional" antibodies and derived fragments, including scFvs. Therefore the instant specification *does not* describe scFv antibodies as single chain antibodies.

Solely to expedite prosecution, and not acquiescing the rejection, claim 1 has been amended to recite that "at least one of the single domain antibodies is an anti-TNF-alpha single domain antibody that binds human TNF-alpha and that comprises CDR 3 of a single domain antibody having the amino acid sequence of SEQ ID NO:12 or SEQ ID NO:13." All of the other remaining rejected claims ultimately depend from claim 1.

Salfeld fails to teach or suggest a single domain antibody that comprises the particularly defined CDR 3. Thus, Salfeld does not anticipate the rejected claims.

Accordingly, reconsideration and withdrawal of the anticipation rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1, 2, 5, 8, 15, 46, and 64-67 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kink et al. (WO 99/64069) ("Kink") in view of Muyldermans (US2007/0031424) ("Muyldermans"). Action at page 10. The Examiner alleged that Kink "disclose[s] methods for treating inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, by oral administration of anti-TNFα antibodies . . . ." *Id.*

The Examiner noted that Kink did not disclose single domain antibodies. *Id.* The Examiner then alleged that Muyldermans "disclose[s] the administration of camelid single domain heavy chain antibodies for the treatment of diseases including Crohn's disease and ulcerative colitis . . . ." *Id.* Finally, according to the Examiner, because single domain antibodies have the advantages of improved expression, solubility, stability and affinity, it would have been obvious to a person of ordinary skill in the art to modify the anti-TNF-alpha antibodies of Kink to be single domain antibodies. *Id.*

Solely to expedite prosecution, and not acquiescing the rejection, claim 1 has been amended to recite that "at least one of the single domain antibodies is an anti-TNF-alpha single

domain antibody that binds human TNF-alpha and that comprises CDR 3 of a single domain antibody having the amino acid sequence of SEQ ID NO:12 or SEQ ID NO:13." All of the other remaining rejected claims ultimately depend from claim 1.

The combination of Kink and Muyldermans does not teach or suggest a single domain antibody that comprises the particularly defined CDR 3. Thus, the combination of Kink and Muyldermans does not render obvious the rejected claims.

Accordingly, reconsideration and withdrawal of the obviousness rejection is respectfully requested.

Double Patenting Rejections

The Examiner provisionally rejected claims 1, 2, 5, 8, 15, 46, and 64-67 as allegedly being unpatentable over claims 26, 28, 30, 34, 36, and 39 of copending Application No. 10/534,348. Applicant notes that the rejection is a provisional rejection. Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

The Examiner provisionally rejected claims 1, 2, 5, 8, 15, 46, and 64-67 as allegedly being unpatentable over claims 13 and 15 of copending Application No. 10/534,349. Applicant notes that the rejection is a provisional rejection. Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

The Examiner provisionally rejected claims 1, 2, 5, 8, 15, 46, and 64-67 as allegedly being unpatentable over claims 20-23, 26, and 28 of copending Application No. 10/553,105. Applicant notes that the rejection is a provisional rejection. Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

The Examiner provisionally rejected claims 1, 2, 5, 8, 15, 46 and 64-67 as allegedly being unpatentable over claims 20, 21, 23, 24, 44, 45, 47 and 48 of copending Application No.

11/788,832 in view of Salfeld et al. (WO 97/29131). Applicant notes that the rejection is a provisional rejection. Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

The Examiner provisionally rejected claims 1, 2, 5, 8, 15, 46, and 64-67 as allegedly being unpatentable over claims 26, 50-59 and 61-67 of copending Application No. 11/636,300 in view of Salfeld et al. (WO 97/29131). Applicant notes that the rejection is a provisional rejection. Applicant may file a terminal disclaimer when the claims are otherwise in allowable format (See MPEP § 804).

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No.: 23/2825, under Docket No.: A0848.70004US00.

Respectfully submitted,

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